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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,569	11/29/2005	Michael Betz	BP/G-32574A/BCK	5279

1095 7590 06/06/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SCHLIENTZ, NATHAN W	
ART UNIT	**PAPER NUMBER**
1616	
MAIL DATE	**DELIVERY MODE**
06/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,569	BETZ ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,7-9,11,12,14,15,18-20 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,7-9,11,12,14,15,18-20 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 4, 6, 10, 13, 16, 17 and 21 have been cancelled by Applicant in a preliminary amendment filed 07 January 2005. Claims 1-3, 5, 7-9, 11, 12, 14, 15, 18-20 and 22-25 are pending. No claim is allowed at this time.

Information Disclosure Statement

The information disclosure statement filed 07 January 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The Foreign Patent Documents EP 0955062, GB 2371227, and WO 01/03741 have been crossed out on the IDS.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 7-9, 11, 12, 14, 15, 18-20 and 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,763,394 (hereinafter O'Connor et al.).

The instant claims are drawn to a multi-dosage liquid pharmaceutical formulation of human growth hormone (hGH) consisting essentially of:

a) about 5 mg/ml to about 100 mg/ml hGH,
b) about 2 mg/ml to about 5 mg/ml phenol,
c) about 5 mM to about 100 mM aqueous buffer,
d) about 0.05 to about 4 mg/ml non-ionic surfactant, and
e) a tonicity-adjusting agent,

wherein the formulation has a tonicity of from about 100 mOsm/kg to about 500 mOsm/kg, pH of from about 6.1 to about 6.3, and is substantially free of an amino acid excipient. Preferably, the aqueous buffer is a phosphate, citrate, acetate, or formate buffer and the non-ionic surfactant is poloxamer 188 or a polysorbate. Most preferably, the aqueous buffer is a phosphate buffer and the non-ionic surfactant is poloxamer 188. The tonicity-adjusting agent is selected from the group consisting of sugar, a sugar alcohol, a polyol and a neutral salt. Preferably, the tonicity-adjusting agent is mannitol.

O'Connor et al. disclose a human growth hormone formulation consisting essentially of (claim 9):

a) 1mg/ml to 20 mg/ml hGH,
b) a preservative,
c) a buffer system to provide a pH of 5.5 to 7,
d) 0.1% w/v to 1% w/v non-ionic surfactant, and
e) 50 mM to 200 mM neutral salt.

O'Connor et al. further disclose the buffer is selected from the group consisting of citrate, phosphate and acetate buffers (claim 16), and is most advantageously in the range of about 2 mM to about 50 mM (column 3, lines 46-48). O'Connor et al. further disclose the non-ionic surfactant is poloxamer 188, poloxamer 184, or polysorbate (claims 11 and 12). O'Connor et al. further disclose that the preferred preservatives

include 0.2-0.4%% w/v phenol (column 3, lines 54 and 55; and claim 17). O'Connor et al. further disclose that about 5 mg/ml to about 50 mg/ml mannitol may be included in the aqueous hGH formulations, as opposed to the neutral salts (column 3, lines 62-64).

O'Connor et al. further disclose a directly injectable hGH formulation consisting essentially of:

a) 5mg/ml hGH,
b) 0.5 mg/ml phenol,
c) 2.5 mg/ml sodium citrate (aqueous buffer),
d) 2.0 mg/ml polysorbate 20 (non-ionic surfactant), and
e) 8.8 mg/ml sodium chloride (neutral salt/tonicity agent),

wherein the hGH formulation is at a pH of 6 (claim 18).

O'Connor et al. further disclose an hGH formulation containing:

a) 5mg/ml hGH,
b) 0.25% w/v phenol,
c) 10 mM sodium citrate (aqueous buffer),
d) 0.1% w/v poloxamer 188 (non-ionic surfactant), and
e) 50 mM mannitol (tonicity adjusting agent).

wherein the hGH formulation is at pH 6.0 (column 7, lines 58-67; and Table 3, Formulation 52).

O'Connor et al. further disclose that the neutral salts concentration is adjusted to near isotonicity, depending on the other ingredients present in the formulation (column 4, lines 1-5).

Therefore, for the aforementioned reasons, O'Connor et al. fully anticipate all the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Connor et al.

Applicant claims:

The Applicant claims a multi-dosage liquid pharmaceutical formulation essentially consisting of:

a) 6.67 mg/ml hGH,
b) 2.5 mg/ml phenol,
c) 10 mM sodium phosphate buffer (aqueous buffer),
d) 30 mg/ml mannitol (tonicity agent), and
e) 2 mg/ml poloxamer 188 (non-ionic surfactant),

wherein the hGH formulation is at a pH of 6.2.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The teachings of O'Connor et al. are described above. Essentially, O'Connor et al. teaches hGH formulations consisting of hGH, phenol, buffer, non-ionic surfactant, and mannitol.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

O'Connor et al. do not explicitly teach an hGH formulation consisting essentially of:

a) 6.67 mg/ml hGH,
b) 2.5 mg/ml phenol,
c) 10 mM sodium phosphate buffer (aqueous buffer),
d) 30 mg/ml mannitol (tonicity agent), and
e) 2 mg/ml poloxamer 188 (non-ionic surfactant),

wherein the hGH formulation is at a pH of 6.2.

However, O'Connor et al. do teach their hGH formulations consisting essentially of:

a) from about 1 mg/ml to about 20 mg/ml hGH (column 3, lines 13-25),
b) 0.2-0.4% (w/v) phenol (column 3, lines 50-56),
c) from about 2 mg/ml to about 50 mM buffer, including phosphate buffer (column 3, lines 46-49),
d) from about 0.1% (w/v) to about 5% (w/v) non-ionic surfactant, including poloxamer 188 (column 3, lines 33-39), and
e) from about 5 mg/ml to about 50 mg/ml mannitol (column 3, lines 62-64).

wherein the formulations have a pH of from about 5.5 to about 7.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to prepare an hGH formulation taught by O'Connor et al., wherein the formulation consists essentially of:

a) 6.67 mg/ml hGH,
b) 2.5 mg/ml phenol,
c) 10 mM sodium phosphate buffer (aqueous buffer),
d) 30 mg/ml mannitol (tonicity agent), and
e) 2 mg/ml poloxamer 188 (non-ionic surfactant),

and having a pH of 6.2, because O'Connor teaches each of the components of the hGH formulation with the suitable ranges that overlap the components of the instantly claimed invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

2. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'Connor et al.

Applicant claims:

The Applicant claims a kit comprising an injection device and a separate container containing a multi-dosage liquid formulation of hGH consisting essentially of:

a) about 5 mg/ml to about 100 mg/ml hGH,
b) phenol,
c) an aqueous buffer, and
d) a non-ionic surfactant,

wherein the hGH formulation is at a pH of about 6.1 to about 6.3.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The teachings of O'Connor et al. are described above. Essentially, O'Connor et al. teaches hGH formulations consisting of from about 1 mg/ml to about 20 mg/ml hGH, phenol, aqueous buffer, and non-ionic surfactant at a pH of from about 5.5 to about 7.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

O'Connor et al. do not explicitly teach a kit comprising the hGH formulation. However, O'Connor et al. do teach a method for using their hGH formulation comprising formulating their composition in a pharmaceutically acceptable, injectable sterile aqueous vehicle, storing said formulation, and directly injecting the stored formulation into a patient (claims 20-23).

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to prepare kit comprising the hGH formulation taught by O'Connor et al., wherein the kit comprises an injectable device and a container with a multi-dosage liquid formulation of hGH because O'Connor et al. teach storing their hGH formulation followed by injecting the formulation into a patient. Thus, the method taught by O'Connor et al. requires the use of an injectable device and a container to store the hGH formulation.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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